

Hereditary Nonpolyposis Colorectal Cancer: Introduction

The [Hereditary Colorectal Cancer Website](#) has been sponsored by the Robert Rauschenberg Foundation

[Hereditary nonpolyposis colorectal cancer \(HNPCC\) syndrome](#) was first described over 100 years ago. It is the most common of the recognized inherited colorectal cancer syndromes. HNPCC is usually characterized by a predisposition to cancer in the third and fourth decades of life, although it is not infrequent to have earlier or later onset. It accounts for approximately 5% of all colon cancer cases. Tumors in patients with HNPCC begin as adenomas and frequently transform to carcinoma. Endometrial, ovarian, urinary tract, biliary tract, small intestine, and gastric cancer are also characteristic of this syndrome and are seen more often in these families with HNPCC than in the general population.

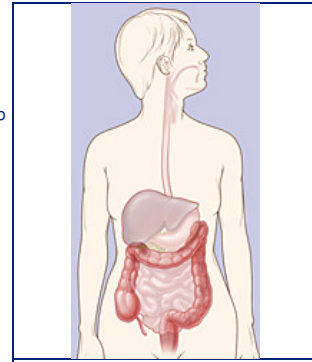


Figure 1. Location of the colon in the body.

What Is Hereditary Nonpolyposis Colorectal Cancer?

HNPCC is also known as Lynch syndrome or cancer family syndrome. HNPCC is a condition in which the tendency to develop colorectal cancer is inherited. "Nonpolyposis" means that colorectal cancer can occur when only a small number of polyps are present (or polyps are not present at all). In families with HNPCC, cancer usually occurs on the right side of the colon. It often occurs at a younger age than colon cancer that is not inherited. Other cancers can occur in these families including cancer of the uterus, ovaries, stomach, urinary tract, small bowel, and bile ducts.

Symptoms

Many patients with colorectal cancer experience no symptoms in the early stage of their disease. In fact, many people have no symptoms until the disease is quite advanced. Therefore, routine colorectal screening and an appreciation of risk factors are extremely important.

Since many of the symptoms of colorectal cancer are also symptoms of a variety of other colon diseases, it is important to see your physician so that the necessary tests can be run and a diagnosis made.

The following is a list of symptoms that may occur:

- Blood in the stool
- Diarrhea that is not the result of diet or illness
- A long period of constipation
- Crampy pain in the abdomen
- Change in bowel habits
- Persistent decrease in the size or caliber of stool
- Frequent feeling of distention in the abdomen or bowel region (gas pain, bloating, fullness, with or without cramping)
- Weight loss with no known reason
- Vomiting and continual lack of energy

Resources

The American Cancer Society

The American Cancer Society
National Headquarters
1599 Clifton Road, N.E.
Atlanta, Georgia 30329
800-ACS-2345
<http://www.cancer.org/>

The ACS can offer assistance if cancer should occur. Check the telephone directory for your local chapter.

State Vocational Rehabilitation Service

This service offers training for another vocation if you should be physically unable to return to the same kind of work performed before the surgery. Check your telephone directory for your state services.

NEWSLETTER: Hereditary Colon Cancer

The NEWSLETTER is a quarterly publication, established in 1984. It deals with hereditary colon cancer and polyposis and is free to all individuals with these conditions and their families. The NEWSLETTER welcomes articles and letters from patients, their families, and professionals. Articles concerning new research and treatment are welcome. This publication may be obtained by contacting:

The Coordinator
Hereditary Cancer Registry
University of Texas M. D. Anderson Cancer Center
Box 78
1515 Holcombe Boulevard
Houston, TX 77030
Phone: 713-792-2828

Hereditary Colorectal Cancer Registries

Registries may be contacted for the names of experts in the management of HNPCC. Registries can also help to identify relatives at risk for the disorder. Further

information concerning Hereditary Colorectal Cancer Registries may be obtained by clicking here or contacting:

Coordinator, Hereditary Colorectal Cancer Registry

The Johns Hopkins Hospital
550 North Broadway, Suite 108
Baltimore, MD 21250-2011
Phone: 1-888-77-COLON
Fax: 410-614-9544
E-mail: hccregistry@jhmi.edu

Cancer Information Service (CIS)

Toll Free: 1-800-4-CANCER

The Cancer Information Service is a national toll-free telephone inquiry system that provides information about cancer and cancer-related resources to the general public, patients and their families, as well as health professionals. Most CIS offices are associated with Comprehensive Cancer Centers or community hospitals. CIS offices do not diagnose or recommend treatment for individuals. They provide support, understanding, and rapid access to the latest information, as well as referral to local services and resources. Printed materials may supplement telephone information. All calls are kept confidential, and individuals do not need to give their names.

The National Society of Genetic Counselors, Inc. (NSGC)

The National Society of Genetic Counselors, Inc. (NSGC)
233 Canterbury Drive
Wallingford, PA 19086-6617
610-872-7608
www.nsgc.org

The National Society of Genetic Counselors is the professional membership association for the genetic counseling profession. NSGC has developed a resource link to assist consumers in locating genetic counseling services.

Hereditary Nonpolyposis Colorectal Cancer: Anatomy

The colon and rectum are part of the digestive tract. The digestive tract is a hollow tube that begins at the mouth and ends at the anus. It has several parts including the esophagus, stomach, small intestine, colon, and rectum (the colon and rectum make up the large intestine).

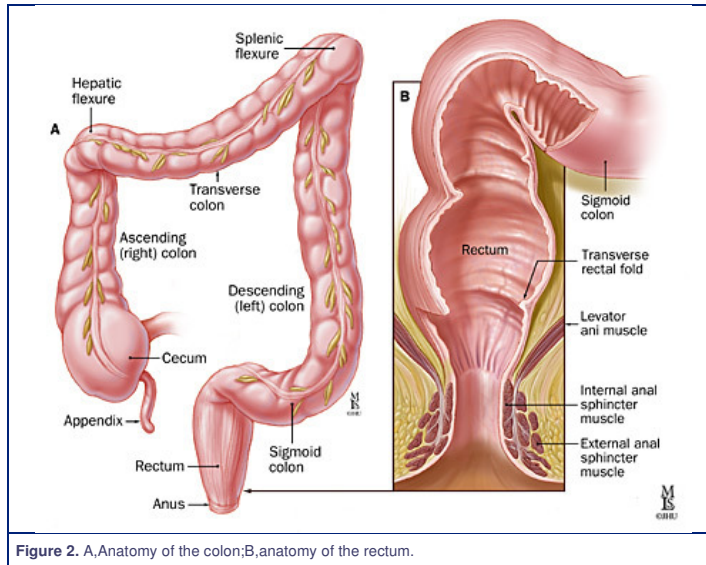


Figure 2. A,Anatomy of the colon;B,anatomy of the rectum.

The intestine is about 28 feet long. The last 5–6 feet of the intestine is called the colon or large intestine. This structure has six major divisions: cecum, ascending colon, transverse colon, descending colon, sigmoid colon, and rectum. The last 5 or 6 inches of the large intestine is the rectum.

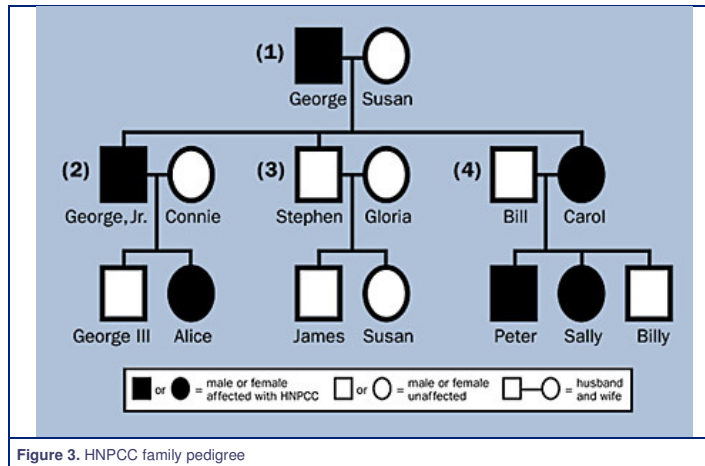
The purpose of the digestive system is to remove nutrients (minerals, vitamins, carbohydrates, proteins, fats, and water) from the foods we eat and to store the waste. After food is digested, solid wastes move through the colon and rectum to the anus, where they are passed out of the body.

Hereditary Nonpolyposis Colorectal Cancer: Causes

How Is HNPCC Inherited?

HNPCC is an autosomal dominant condition. This means that people with HNPCC have a 50% chance of passing the HNPCC gene mutation (change) to each of their children. The gene mutation can be passed on even if the parent has had surgery to remove his or her own colon. Individuals who do not inherit the gene mutation cannot pass it to their own children. The vast majority of individuals with HNPCC develop cancer (Figure 1).

Some individuals with HNPCC do not have an affected parent. These individuals, who are the first in the family to have the condition, are referred to as having a new mutation (newly altered gene). They can, however, pass this HNPCC gene mutation to their children.



(1) George has HNPCC, his wife, Susan, is unaffected. They have three children, George, Jr., Stephen, and Carol. All were at 50% risk of developing HNPCC. George, Jr. and Carol are affected.

(2) George, Jr. and his wife, Connie, have two children. Both children had a 50% chance of inheriting HNPCC. Their daughter, Alice is affected.

(3) Stephen and his wife Gloria have two children. Because Stephen is unaffected there was no risk to his children of developing HNPCC.

(4) Carol and Bill have three children. Each child had a 50% chance of inheriting HNPCC and two are affected; son Billy is not.

Genetic counseling is available, and recommended, for individuals with HNPCC and their family members. Genetic counselors will explain the inheritance pattern of HNPCC, discuss which family members are at risk for developing the condition, and provide necessary information regarding genetic testing. Counseling services are available through genetic and oncology departments in many hospitals. To make an appointment with a member of the Johns Hopkins professional medical team or to speak with someone at the Colorectal Cancer Risk Assessment Service, please call (410) 614-LIFE (5433). Also, it is recommended that HNPCC families contact registries for access to resources and for help with identification of family members at risk.

Hereditary Nonpolyposis Colorectal Cancer: Diagnosis

Why Is Early Diagnosis Important?

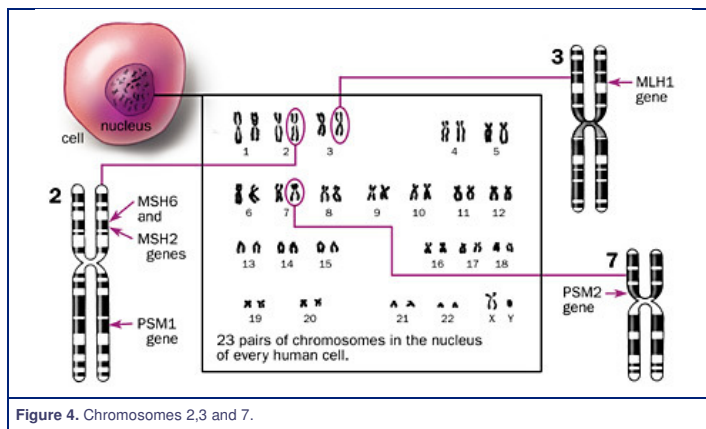
Early diagnosis is important for early detection and prevention of cancer. Regular screening should start at the ages described in the exam guidelines below. When colorectal cancer is detected early, the chance of cure is much better.

How Is HNPCC Diagnosed?

Persons at risk for HNPCC usually have a family history of two successive generations with colorectal cancer or at least one generation with colorectal cancer and one generation with polyps. Men and women at risk for HNPCC need examinations of the entire colon. Women at risk should also have yearly endometrial and ovarian screening. Tests such as colonoscopy and barium enema with flexible sigmoidoscopy are available to tell whether polyps or cancer are present in the colon. For patients at risk for HNPCC, colonoscopy is the preferred method of screening.

Genetic Testing

Mutations (alterations) of one of five genes are now known to be responsible for most cases of HNPCC. These genes are called hMSH2, hPMS1, MSH6 (all on chromosome 2), hMLH1 (chromosome 3), and hPMS2 (chromosome 7). Other genes, presently undiscovered, may also cause HNPCC. Gene tests for HNPCC are available for selected individuals from families who have HNPCC. A family member affected with colon cancer should be tested first, whenever possible.



The test requires a small blood sample. The gene test results will influence the future management of individuals who are at risk for HNPCC. For example, if the test shows that a person does not have the gene mutation known in the family, he or she can avoid many unnecessary colon examinations. If the test shows that a person does have the gene mutation, then the physician will need to be alerted to schedule annual colonoscopies and follow screening guidelines.

Microsatellite Instability Testing

Microsatellite instability (MSI) testing is used as a screening test to see how likely it is that a person's cancer was caused by one of the genes associated with HNPCC. It is usually done on colon tumor tissue that is removed and stored as part of the normal process when a person has surgery for colon cancer.

If the tumor tissue tests MSI positive, it is considered more likely that the cancer is due to one of the HNPCC gene mutations. People who have a positive MSI test have the option to pursue the genetic blood test. If the tumor tissue tests MSI negative, however, it is highly unlikely that current genetic testing will be helpful for the affected person's family. An MSI negative test result does not rule out the diagnosis of HNPCC.

Exam Guidelines

For People Who Have Had HNPCC Gene Testing

The following three outcomes are possible.

1. **Positive gene test**—an HNPCC gene mutation was found in a person's blood sample.

Persons with a positive gene test should have a colonoscopy every year and follow the exam guidelines for people at risk listed below. In addition, other ways to prevent cancer, surgeries such as colectomy, hysterectomy, and oophorectomy, may be considered.

2. **Negative gene test**—No HNPCC gene mutation was found in a person's blood sample and an affected family member has had a positive gene test.

Persons with a negative gene test (an HNPCC gene mutation was not found), require careful evaluation by their doctor and a genetic counselor to determine the best screening guidelines to follow.

3. **No mutation found**—No HNPCC gene mutation was found in a person's blood sample and no affected family member has had a positive gene test.

Continue to follow screening guidelines for persons with a family history of colorectal cancer.

At this time, the available gene tests cannot detect all HNPCC-causing genes. Future advances in technology, such as the Conversion method, may provide more accurate diagnosis. A genetic counselor or physician will assist in finding a laboratory that provides the best testing

For People at Risk Who Have Not Had HNPCC Gene Testing

1. Colonoscopy every 1–2* years starting by age 25 years or 5–10 years before the age of earliest colorectal cancer diagnosed in the family, whichever is younger. At age 40 begin annual colonoscopy.
2. Annual stool hemocult tests, urinalysis, and blood tests for liver function starting when colonoscopy begins.
3. For women: yearly pelvic exam with Pap test and transvaginal ultrasound of the uterus and ovaries or Pipel biopsy starting at age 25 and continuing annually.
4. Consider annual upper endoscopy in families with gastric cancer.

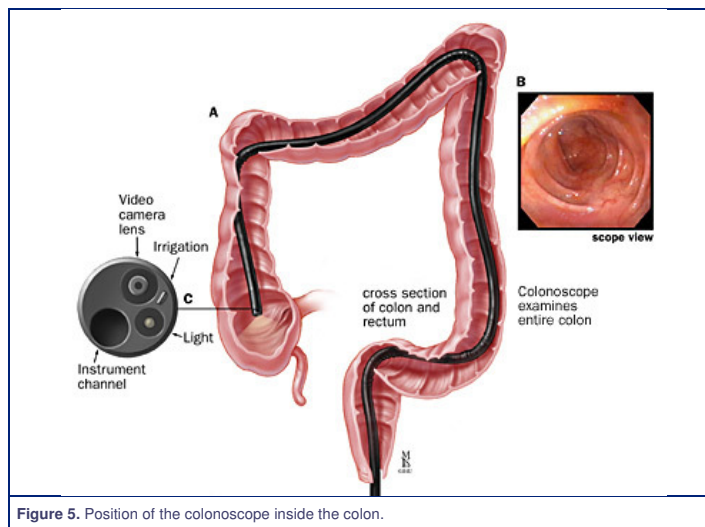
*Colonoscopy is recommended every year for a person with a positive gene test.

If colon polyps or cancer is found, follow the treatment guidelines.

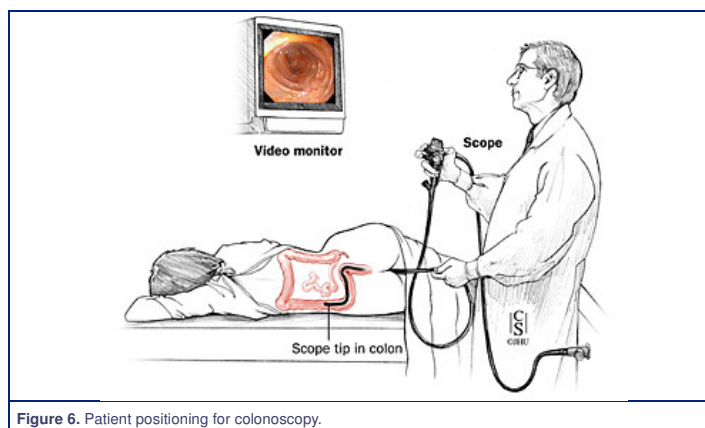
Colonoscopy

A colonoscopy is an examination of the rectum and the entire colon. It is performed with a lighted, flexible, hollow tube, which is slightly larger in diameter than an enema tube. Colonoscopy permits the doctor to see much farther into the bowel than sigmoidoscopy.

The colonoscope allows the doctor to see whether polyps or cancer are present.



A biopsy forceps may be inserted through a channel in the colonoscope to remove a small sample of tissue for microscopic examination. Sometimes it is necessary for the doctor to introduce air into the colon to improve visibility. Before having a colonoscopy the colon must be clear of stool so that the doctor has good visibility. The patient must undergo a preparation that may include a liquid diet, enema, and laxatives to clear stool from the colon. The technique for bowel preparation may differ by health facility.



A sedative is given before a person undergoes colonoscopy. Many people sleep through the whole procedure and feel little or no discomfort. Occasionally, the insertion of air during the procedure may cause the same kind of discomfort as gas pain.

Hereditary Nonpolyposis Colorectal Cancer: Therapy

Endoscopic Therapy

If a polyp is found, removal through colonoscope may be sufficient, although surgery may be recommended for some patients. If cancer is found at examination, the doctor will recommend colorectal surgery.

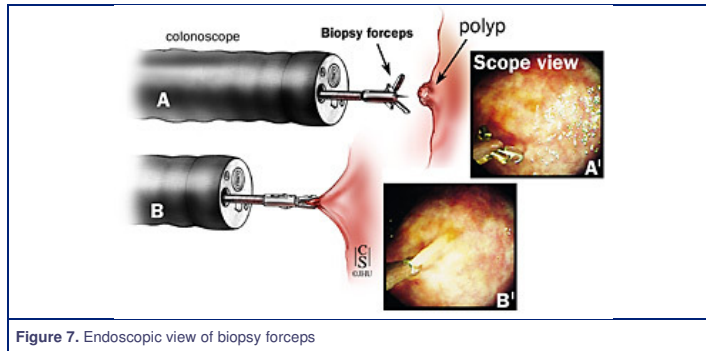


Figure 7. Endoscopic view of biopsy forceps

Surgical Therapy

If cancer is found at examination, the doctor will recommend colorectal surgery. Removing the entire colon is the only way to completely prevent the development of colon cancer or to treat existing cancer. Proctocolectomy and colectomy, demonstrated below, show the difference between having both colon and rectum removed and having just colon removed, while the rectum remains intact.

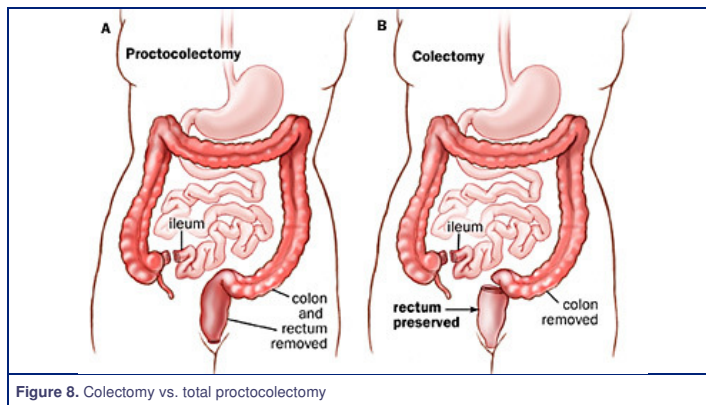


Figure 8. Colectomy vs. total proctocolectomy

Several different operations are currently available for treatment of HNPCC. The three most commonly performed operations are:

1. Total proctocolectomy with Brooke ileostomy (with pouch)
2. Colectomy with ileorectostomy
3. Restorative proctocolectomy (ileoanal pouch procedure)

All three operations involve removal of all or most of the colon. After a complete discussion of these operations, the patient and surgeon together can decide which one is best. Women with HNPCC may also consider surgical removal of the uterus, ovaries, and fallopian tubes.

Total Proctocolectomy with Brooke ileostomy (with pouch)

This procedure involves complete removal of the entire colon and rectum. The end of the small intestine is brought out as an ileostomy. Although the restorative proctocolectomy is the preferred procedure in most cases, total proctocolectomy with Brooke ileostomy is generally performed in situations when invasive cancers are present in the rectum, when the anal sphincter is not functioning correctly, or in elderly patients in whom strength of the sphincter muscles is diminished.

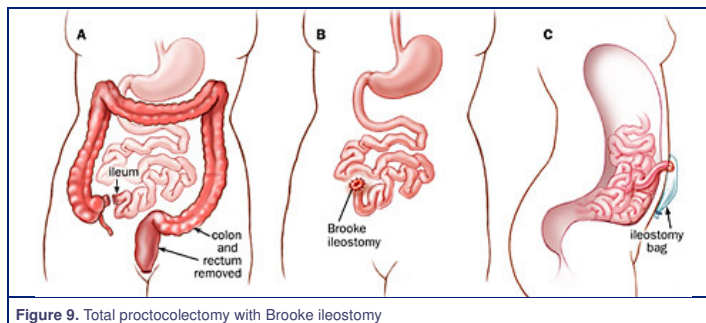
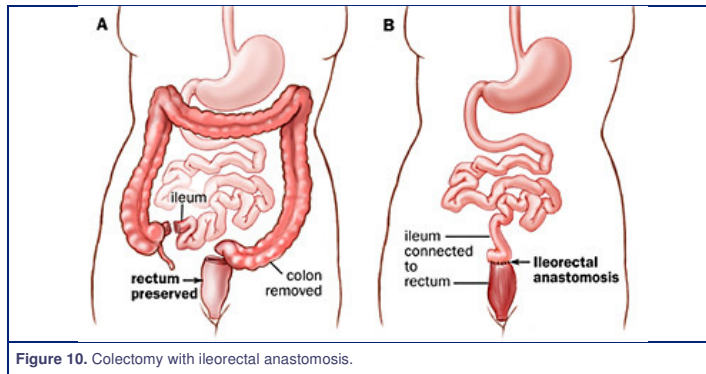


Figure 9. Total proctocolectomy with Brooke ileostomy

Colectomy with ileorectostomy

In this procedure, the colon is removed but all or most of the rectum is preserved. The small intestine is attached to the upper portion of the rectum. The advantage of the ileorectalostomy procedure is that it is a less complicated, one-stage operation, yet still preserves fecal continence and maintains tolerable bowel function. The main concern with this procedure is that the rectum is left in place, despite its potential propensity for the development of polyps and cancer. Colectomy with ileorectal attachment is generally performed in patients who have few or no polyps in the rectum. In this case, often the remaining rectum requires frequent surveillance and removal of premalignant polyps.



Restorative Proctocolectomy (Ileoanal Pouch Procedure)

The restorative proctocolectomy involves removal of the entire colon and most of or the entire rectum. The end of the small intestine (ileum) is attached to the very distal rectum with the creation of an ileal pouch. With this operation, either a small portion of rectal mucosa can be left intact or the remainder of the rectal lining can be stripped. In this way, continence can be maintained and yet all or nearly all of the at-risk large intestinal lining can be removed. The ileal pouch provides a reservoir for fecal storage. Typically, the operation is performed in two stages. In the first stage a temporary ileostomy is created. After a period of time the ileostomy is removed to direct the intestinal stream during the healing of the ileoanal pouch. Alternatively some medical centers favor a single-stage procedure where no temporary ileostomy is used.

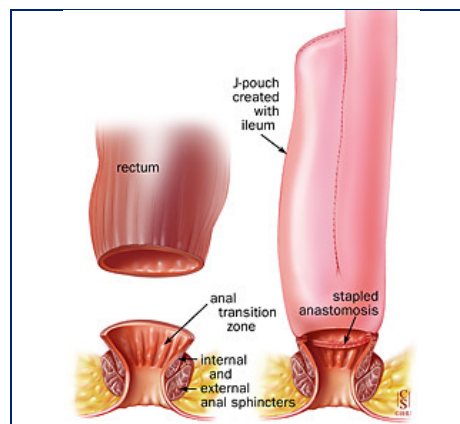
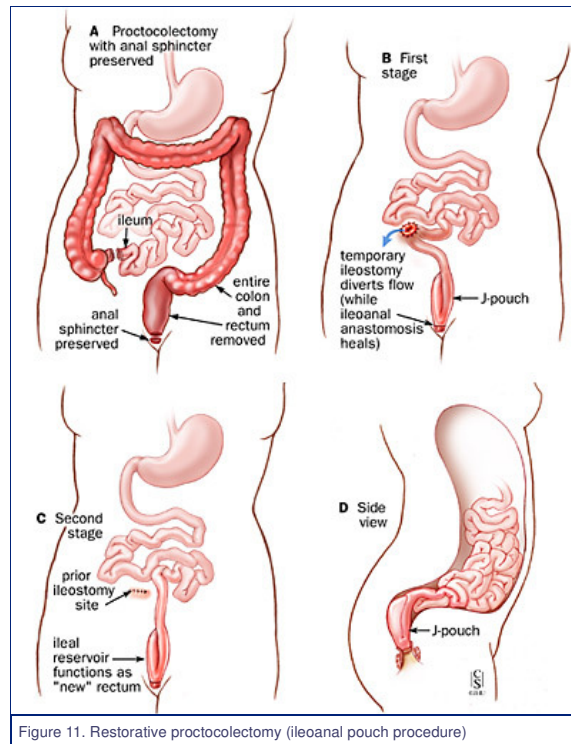


Figure 12. Ileal pouch anal anastomosis (mucosal lining left intact)

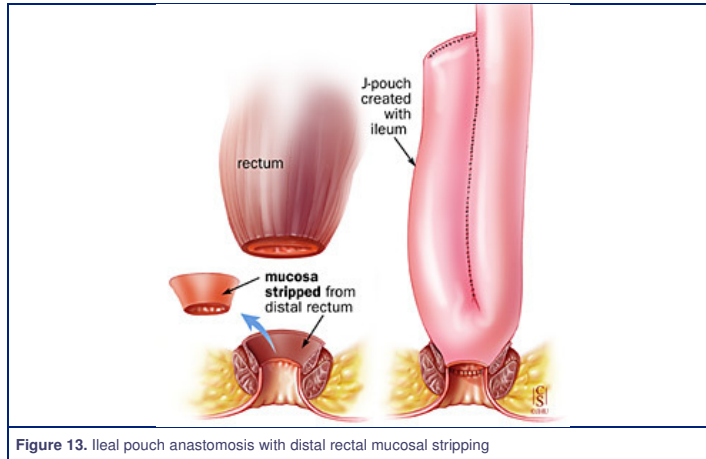


Figure 13. Ileal pouch anastomosis with distal rectal mucosal stripping

All operations involve removal of all or most of the colon. After a complete discussion of these operations, the patient and surgeon together can decide which one is best.

In some cases, after colon removal, a person may have an ileostomy. An ileostomy is an opening on the abdomen through which stool leaves the body. An ileostomy can be temporary or permanent. In most cases it is necessary to wear an appliance called an ileostomy bag to collect body wastes. An ileostomy should not be considered a handicap, although it is an inconvenience. With proper care, there should be no odor or uncleanness. Thousands of people of every age and of both sexes have had ileostomy surgery. After surgery, people can be just as busy, successful, and involved in daily routines as before surgery. In fact, they may be more active because of improved health.

Lifestyle After Surgery

Sexual function is not impaired after surgery or ileostomy. It is important that both partners understand the surgery, by talking with the surgeon or the family physician. There is usually no need for change in established sex practices or in one's capacity to enjoy sexual intercourse. It is also possible to have successful pregnancies. However, a woman who plans to become pregnant should consult her physician before becoming pregnant. Physicians usually recommend that a woman wait about a year after a colorectal operation before becoming pregnant. This delay gives plenty of time for abdominal scars to heal soundly and for the woman's health to return to normal. An ileostomy should not harm the baby or endanger the mother during childbirth.

Overview

For families with HNPCC, the most common complication seen is the presence of cancer in organs other than the colon. This includes cancer of the uterus, ovary, stomach, urinary tract, small bowel, and bile ducts.